Clinical Studies

In a 2005 study report in the International Journal of Cancer an experiment was done were they fed rats flaxseeds and Lung metastasis was reduced up to 70%

In the November 2004 issue of Clinical Cancer Research, a study was done combining flaxseed with tamoxifen and another group with tamoxifen alone. The study reported: "They used mice injected with human breast cancer tumors and the tumors in the flaxseed fed mice shrunk 74%.

The tamoxifen produced a similar effect to the flaxseed shrinking the tumors initially, but by the end of the experiment, the tumors had returned to their initial size using just tamoxifen.

The study reported:

"The women who eat the most flax lowered their risk of getting breast cancer by 62% compared to women who do not eat it. Women with this genetic marker who eat large amounts of flax lignans reduce their risk of breast cancer by up to 70%."

The secret of the Budwig oil and cottage cheese mixture that Dr. Budwig used is that it contains two anticancer components: lignans and an omega-3 fat called "alphalinolenic acid" (ALA).

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4077601/
https://www.ncbi.nlm.nih.gov/pubmed/15897583

The buzz on flax seeds and breast cancer

Jacob Schor
November 30, 2006

Subject: flax seeds and breast cancer

[i]Far more pertinent and relevant information comes from studies in which human breast cancers were implanted into animals, or chemically induced. Saarinen et al reported in August of 2002 that lectins from flax seed inhibited the formation and growth of tumors triggered in rats by dosing with the carcinogen DMBA.

[ii] Wang et al. reported in 2005 study in the International Journal of Cancer on their work injecting estrogen receptor negative breast cancer cells into rats fed various flaxseed fractions to determine whether it was the lignan, oil or other components. Feeding the rats any combination of flax extracts produced beneficial effect. Tumor growth rate was significantly lower in all of the flax fed rats due to decreased cell proliferation and increased apoptosis; Lung metastasis incidence was reduced (16-70%) by all treatments; distant lymph node metastasis was significantly decreased (52%) only in the flax oil group. Total metastasis incidence was lowered (42%) in the lignan combined with flax oil fed rats.

[iii]In the November, 2004 issue of Clinical Cancer Research, Chen et al. described their experiments investigating the effect of flaxseed in combination with tamoxifen and alone. They used mice with human breast cancer tumors with and without supplemental estrogen. At low estrogen levels, predictive of a woman in menopause, tumors in the flaxseed fed mice shrunk 74%. The tamoxifen produced a similar effect to the flaxseed shrinking the tumors initially, but by the end of the experiment, the tumors had returned to their initial size. Combining tamoxifen and flaxseed shrunk the tumor half again as much as tamoxifen alone did. In the mice kept at high estrogen levels, modeling a premenopausal breast cancer patient, the flaxseed alone inhibited tumor growth by 22%. The tamoxifen alone inhibited tumor growth by 41% and both together by 50%.

Tamoxifen increases the risk of uterine cancer in humans by eight times. It caused the uterus of these test mice to swell by 39%. Flax seed prevented the tamoxifen from causing this uterine growth. Flaxseed on its own inhibited estrogen receptor positive breast cancer and increased the effectiveness of tamoxifen and possibly prevent uterine cancer, a known risk associated with using this drug treatment.

[iv] In 2002 Chen et al writing in Nutrition and Cancer described another experiment in which they injected human breast cancer cells into mice. Half the mice were given flax seed. The flax fed mice had half the incidence of tumor metastasis. Lung metastasis was 56% in the control group and only 22.2% in the flax fed mice. Flax seed decreased lymph node metastasis from 89% to 33%. Lung tumors decreased by 82%. The researchers showed that these effects were partly due to flax seeds effect of decreasing insulin-like growth factor I and epidermal growth factor receptor expression.

[v] Also in November 2002, Dabrosin et al published in Cancer Letters a study suggesting that flaxseed inhibited angiogenesis in breast tumors by decreasing levels of vascular endothelial growth factor (VEGF) which is a key factor in breast cancer angiogenesis.

[vi] It strongly hints that flax seed may have a role in treating other cancers as well.

Flax seeds inhibit breast tumor growth whether the tumor is estrogen receptor positive or negative. The theory that flax seeds work because they block estrogen receptors does not hold up. Something else is going on.

In May of 2005 researchers moved from reporting on rats and mice to reporting on flax seed interventions in people. Thompson et al reported in Clinical Cancer Research on a study involving women recently diagnosed with breast cancer who were awaiting breast surgery. For the three weeks between their initial biopsy and diagnosis to their surgeries, the women in the experiment ate a muffin with 25 grams of flax seed hidden in it. The control group ate muffins without flax seeds. The tumors in the women eating the flax muffins were noticeably changed in just these three weeks. The tumors had 31% more dying cancer cells in them, a 34% decrease in growth and a 71% decrease in HER2/Neu expression. Her2/Neu is a genetic marker that predicts more aggressive cancers.

[vii] Other human research shows that flax seeds change the way estrogen is broken down and eliminated from the body. Eating flax seeds increases the breakdown of estrogen into the good 2-OH forms and reduces the bad 16-OH estrogens. Other fibers like wheat bran do not do this.

[viii] Neither does soy.

[ix] Shifting these estrogen metabolites to greater amounts of the 2/good estrogen is important because it reduces risk of breast cancer.

[x] The more flax she eats, the less likely a woman will get breast cancer. The women who eat the most flax lower their risk of getting breast cancer by 62% compared to women who do not eat it. [xi] Flax consumption in epidemiological reviews produces a greater protective effect premenopausally.

[xii] Women with a genetic variant of the CPY17 gene have an increased risk for breast cancer. Women with this genetic marker who eat large amounts of flax lignans reduce their risk of breast cancer by up to 70%.

[xiii] , [xiv] Credit for this article must be given to the esteemed Michael Uzick, ND who provided me with both inspirational outrage and the references to back the information in this article.

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[i] Int J Cancer. 2006 Nov 15;119(10):2279-86. Links

Maternal dietary exposure to fiber during pregnancy and mammary tumorigenesis among rat offspring.

- ✓ Yu B ,
- ✓ Khan G ,
- ✓ Foxworth A ,
- ✓ Huang K ,
- ✓ Hilakivi-Clarke L .

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Maternal diet during pregnancy has been proposed to modify female offspring's later susceptibility to develop breast cancer; however, most of the dietary factors identified thus far have led to increased risk. To identify dietary factors that might reduce offspring's breast cancer risk, pregnant rat dams were fed diets containing 6% fiber originating either from cellulose (control), or oat, whole wheat or defatted flax flour. At birth, dams were switched to the AIN93 semi-purified diet. Mammary tumor incidence and multiplicity, induced by administering the offspring 5 mg 7,12-dimethylbenz[a]anthracene (DMBA) at the age of 50 days, was reduced in the whole wheat flour-exposed offspring and increased in the defatted flax-exposed offspring. To identify the mechanisms mediating the effects of in utero dietary exposures, changes in mammary gland morphology and gene expression were assessed before puberty onset (3 weeks of age) and at the time rats are most susceptible to malignant transformation (8 weeks of age). The number of terminal end buds (TEBs), i.e., the targets of malignant transformation, was reduced in the mammary glands of whole wheat- and oat flour-exposed offspring, as compared to the controls. Further, the number of apoptotic epithelial cells (based on ISOL assay) was elevated in the whole wheat flour offspring, but no changes in cell proliferation (PCNA), estrogen receptor alpha (ER-alpha) or cyclin D1 mRNA or protein levels were seen. The mRNA and/or protein levels of BRCA1 and p53 were significantly increased in the mammary glands of whole wheat flour offspring. Further, the levels of 8-hydroxy-2'-deoxyguanosine (8-OHdG), a marker of DNA damage, were significantly reduced in these rats, suggesting that maternal dietary exposure to whole wheat during pregnancy may reduce offspring's breast cancer risk by improving DNA damage repair mechanisms.

PMID: 16921499

[ii] Mol Cancer Ther. 2002 Aug;1(10):869-76. Links

Enterolactone inhibits the growth of 7,12-dimethylbenz(a)anthracene-induced mammary carcinomas in the rat.

- ✓ Saarinen NM ,
- ✓ Huovinen R ,
- ✓ Warri A ,
- ✓ Makela SI ,
- ✓ Valentin-Blasini L ,
- ✓ Sjoholm R ,
- ✓ Ammala J ,
- ✓ Lehtila R ,
- ✓ Eckerman C ,
- ✓ Collan YU ,
- ✓ Santti RS .

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The inverse association between a high enterolactone (ENL) concentration in both urine and serum, and the risk of breast cancer found in epidemiological studies suggests a chemopreventive action for ENL. However, no causal relationship has been established in clinical studies or in experimental models for breast cancer. In the present study, the potential chemopreventive action of p.o. administered ENL (1 or 10 mg/kg of body weight) was tested in 7,12-dimethylbenz(a)anthracene-induced mammary cancers of the rat. Rats were maintained on a standard open-formula chow diet. Daily p.o. administration of ENL at a dose of 10 mg/kg of body weight for 7 weeks significantly inhibited tumor growth. The growth-inhibitory effect of ENL was more pronounced on the new tumors, which developed during the treatment period, but ENL also inhibited the growth of those tumors established before the start of the lignan administration. The rat serum concentration of ENL, which illustrated a permanent positive effect on breast cancer growth, was 0.4 microM, which is >10-fold as compared with the serum concentrations found in the general human population. The effect of ENL was not restricted to any specific histological tumor type. ENL was demonstrated to act as a weak aromatase inhibitor in vitro and to reduce the relative uterine weight of the 7,12-dimethylbenz(a)anthracene-treated nonovariectomized rats. However, in a short-term assay ENL had no effect on the uterine growth of the intact or androstenedione-treated immature rats. Thus, the mechanism of the ENL action and its minimum or optimal daily dose remains to be clarified.

PMID: 12492120 [PubMed – indexed for MEDLINE]

[iii] Int J Cancer. 2005 Sep 20;116(5):793-8. Links

The inhibitory effect of flaxseed on the growth and metastasis of estrogen receptor negative human breast cancer xenograftsis attributed to both its lignan and oil components.

- ✓ Wang L ,
- ✓ Chen J ,
- ✓ Thompson LU .

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Our previous studies have shown that dietary flaxseed (FS) can reduce the growth and metastasis of human estrogen receptor negative (ER-) breast cancer in nude mice. The aims of our study were to determine (i) whether the tumor inhibitory effect of FS was due to its oil (FO), lignan secoisolariciresinol diglycoside (SDG), or both components, and (ii) whether the effect on tumor growth was related to increased lipid peroxidation. Athymic nude mice were orthotopically injected with ER- breast cancer cells (MDA-MB-435) and 8 weeks later were fed either the basal diet (BD) or BD supplemented with 10% FS, SDG, FO, or combined SDG and FO (SDG + FO) for 6 weeks. The SDG and FO levels were equivalent to the amounts in the 10% FS. Compared to the BD group, the tumor growth rate was significantly lower (p < 0.05) in the FS, FO, and SDG + FO groups, in concordance with decreased cell proliferation and increased apoptosis; however, these did not significantly relate to the lipid peroxidation, indexed as malonaldehyde (MDA), in the primary tumors. Lung metastasis incidence was reduced (16-70%) by all treatments, significantly in the FS and SDG + FO groups. The distant lymph node metastasis was significantly decreased (52%) only in the FO group. Although the total metastasis incidence was lowered (42%) significantly only in the SDG + FO group, all treatment groups did not differ significantly. In conclusion, FS reduced the growth and metastasis of established ER- human breast cancer in part due to its lignan and FO components, and not to lipid peroxidation. (c) 2005 Wiley-Liss, Inc.

PMID: 15849746 [PubMed – indexed for MEDLINE]

[iv] Clin Cancer Res. 2004 Nov 15;10(22):7703-11. Links

Dietary flaxseed enhances the inhibitory effect of tamoxifen on the growth of estrogen-dependent human breast cancer (mcf-7) in nude mice.

- ✓ Chen J ,
- ✓ Hui E ,
- ✓ Ip T ,
- ✓ Thompson LU .

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PURPOSE: This study determined the effect of 10% dietary flaxseed (FS) and tamoxifen (TAM), alone and in combination, on the growth of estrogen-dependent human breast cancer (MCF-7) in athymic mice with or without 17beta-estradiol (E2) supplementation. EXPERIMENTAL DESIGN: Ovariectomized mice received injection with MCF-7 cells, were implanted with an E2 pellet (1.7 mg), and fed the basal diet (BD). When tumor reached approximately 40 mm2, the E2 implant was removed, and mice were randomized to the following groups and maintained at either low (E2 pellet removed) or high E2 level (new E2 pellet implanted) for 6 weeks: (a) positive control with new E2 pellet, fed BD, (b) negative control with no E2 implant, fed BD, (c) TAM group with TAM pellet (5 mg) implant, fed BD, (d) FS group fed 10% FS, (e) FS+TAM group with TAM implant, fed 10% FS. Tumor growth was monitored weekly. RESULTS: At low E2 level, FS regressed the pretreatment tumor size by 74%. TAM regressed tumor initially but later induced an increase so that the tumor size was finally similar to the pretreatment size. A tumor regression >53% was induced by FS+TAM than by TAM alone. At high E2 level, FS, TAM, and FS+TAM inhibited the tumor growth by 22, 41, and 50%, respectively, compared with the positive control. Decreased tumor size was attributable to reduced tumor cell proliferation and increased apoptosis. CONCLUSIONS: FS inhibited the growth of human estrogen-dependent breast cancer and strengthened the tumor-inhibitory effect of TAM at both low and high E2 levels.

PMID: 15570004 [PubMed – indexed for MEDLINE]

[v] Nutr Cancer. 2002;43(2):187-92. Links

Dietary flaxseed inhibits human breast cancer growth and metastasis and downregulates expression of insulin-like growth factor and epidermal growth factor receptor.

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- ✓ Stavro PM ,
- ✓ Thompson LU .

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Recent studies indicate that diets rich in phytoestrogens and n-3 fatty acid have anticancer potential. This study determined the effect of flaxseed (FS), the richest source of lignans and alpha-linolenic acid, on growth and metastasis of established human breast cancer in a nude mice model. Estrogen receptor-negative human breast cancer cells, MDA-MB-435, were injected into the mammary fat pad of mice (Ncr nu/nu) fed a basal diet (BD). At Week 8, mice were randomized into two diet groups, such that the groups had similar tumor size and body weight. One continued on the BD, while the other was changed to BD supplemented with 10% FS, until sacrifice at Week 15. A significant reduction (P < 0.05) in tumor growth rate and a 45% reduction (P = 0.08) in total incidence of metastasis were observed in the FS group. Lung metastasis incidence was 55.6% in the BD group and 22.2% in the FS group, while the lymph node metastasis incidence was 88.9% in the BD group and 33.3% in the FS group (P < 0.05). Mean tumor number (tumor load) of total and lymph node metastasis was significantly lower in the FS than in the BD group (P < 0.05). Metastatic lung tumor number was reduced by 82%, and a significantly lower tumor trend (P < 0.01) was observed in the FS group. Lung weight, which also reflects metastatic tumor load, in the FS group was reduced by 20% (P < 0.05) compared with the BD group. Immunohistochemical study showed that Ki-67 labeling index and expression of insulin-like growth factor I and epithelial growth factor receptor in the primary tumor were lower in the FS (P < 0.05) than in the BD group. In conclusion, flaxseed inhibited the established human breast cancer growth and metastasis in a nude mice model, and this effect is partly due to its downregulation of insulin-like growth factor I and epidermal growth factor receptor expression.

PMID: 12588699 [PubMed – indexed for MEDLINE]

[vi] Cancer Lett. 2002 Nov 8;185(1):31-7. Links

Flaxseed inhibits metastasis and decreases extracellular vascular endothelial growth factor in human breast cancer xenografts.

- ✓ Dabrosin C ,
- ✓ Chen J ,
- ✓ Wang L ,
- ✓ Thompson LU .

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Angiogenesis is important in tumor growth, progression and metastatic dissemination. Vascular endothelial growth factor (VEGF) is one key factor in promotion of breast cancer angiogenesis. VEGFs are bioactive in the extracellular space where they become available to the endothelial cells. Phytoestrogens such as lignans have been shown to alter breast cancer incidence and be cancer-protective in rats. We show that supplementation of 10% flaxseed, the richest source of mammalian lignans, to nude mice with established human breast tumors reduced tumor growth and metastasis. Moreover, flaxseed decreased extracellular levels of VEGF, which may be one mechanistic explanation to the decreased tumor growth and metastasis.

PMID: 12142076 [PubMed – indexed for MEDLINE]

[vii] Clin Cancer Res. 2005 May 15;11(10):3828-35. Links

Dietary flaxseed alters tumor biological markers in postmenopausal breast cancer.

- ✓ Thompson LU ,
- ✓ Chen JM ,
- ✓ Li T ,
- ✓ Strasser-Weippl K ,
- ✓ Goss PE .

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PURPOSE: Flaxseed, the richest source of mammalian lignan precursors, has previously been shown to reduce the growth of tumors in rats. This study examined, in a randomized double-blind placebo-controlled clinical trial, the effects of dietary flaxseed on tumor biological markers and urinary lignan excretion in postmenopausal patients with newly diagnosed breast cancer. EXPERIMENTAL DESIGN: Patients were randomized to daily intake of either a 25 g flaxseed-containing muffin (n = 19) or a control (placebo) muffin (n = 13). At the time of diagnosis and again at definitive surgery, tumor tissue was analyzed for the rate of tumor cell proliferation (Ki-67 labeling index, primary end point), apoptosis, c-erbB2 expression, and estrogen and progesterone receptor levels. Twenty-four-hour urine samples were analyzed for lignans, and 3-day diet records were evaluated for macronutrient and caloric intake. Mean treatment times were 39 and 32 days in the placebo and flaxseed groups, respectively. RESULTS: Reductions in Ki-67 labeling index (34.2%; P = 0.001) and in c-erbB2 expression (71.0%; P = 0.003) and an increase in apoptosis (30.7%; P = 0.007) were observed in the flaxseed, but not in the placebo group. No significant differences in caloric and macronutrient intake were seen between groups and between pre- and posttreatment periods. A significant increase in mean urinary lignan excretion was observed in the flaxseed group (1,300%; P < 0.01) compared with placebo controls. The total intake of flaxseed was correlated with changes in c-erbB2 score (r = -0.373; P = 0.036) and apoptotic index (r = 0.495; P < 0.004). CONCLUSION: Dietary flaxseed has the potential to reduce tumor growth in patients with breast cancer.

PMID: 15897583 [PubMed – indexed for MEDLINE]

[viii] Cancer Epidemiol Biomarkers Prev. 2000 Jul;9(7):719-25. Links

The effect of flaxseed and wheat bran consumption on urinary estrogen metabolites in premenopausal women.

- ✓ Haggans CJ ,
- ✓ Travelli EJ ,
- ✓ Thomas W ,
- ✓ Martini MC ,
- ✓ Slavin JL .

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Estrogen is metabolized along two competing pathways to form the 2-hydroxylated and the 16alpha-hydroxylated metabolites. Based on proposed differences in biological activities, the ratio of these metabolites, 2-hydroxyestrogen:16alpha-hydroxyestrogen (2:16alpha-OHE1), has been used as a biomarker for breast cancer risk. Women with an elevated 2:16alpha-OHE1 ratio are hypothesized to be at a decreased risk of breast cancer. Flaxseed, the most significant source of plant lignans, and wheat bran, an excellent source of dietary fiber, have both been shown to have chemoprotective benefits. Some of these benefits may be attributable to their influence on endogenous sex hormone production and metabolism. We examined the effect of flaxseed consumption alone and in combination with wheat bran on urinary estrogen metabolites in premenopausal women. Sixteen premenopausal women were studied for four feeding treatments lasting two menstrual cycles each in a randomized cross-over design. During the four feeding treatments, subjects consumed their usual diets supplemented with baked goods containing no flaxseed or wheat bran, 10 g of flaxseed, 28 g of wheat bran, or 10 g of flaxseed plus 28 g of wheat bran. Urinary excretion of 2-hydroxyestrogen and 16alpha-hydroxyestrone, as well as their ratio, 2:16alpha-OHE1, were measured by enzyme immunoassay. Flaxseed supplementation significantly increased the urinary 2:16alpha-OHE1 ratio (P = 0.034), but wheat bran had no effect. These results suggest that flaxseed may be chemoprotective in premenopausal women.

PMID: 10919743 [PubMed – indexed for MEDLINE]

[ix] Am J Clin Nutr. 2004 Feb;79(2):318-25. Links

Supplementation with flaxseed alters estrogen metabolism in postmenopausal women to a greater extent than does supplementation with an equal amount of soy.

- ✓ Brooks JD ,
- ✓ Ward WE ,
- ✓ Lewis JE ,
- ✓ Hilditch J ,
- ✓ Nickell L ,
- ✓ Wong E ,
- ✓ Thompson LU .

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BACKGROUND: Phytoestrogens, which are abundant in flaxseed and soy, have chemical structures resembling those of endogenous estrogens and have been shown to exert hormonal effects, thereby affecting chronic diseases. OBJECTIVE: We compared the effects of consuming equal amounts of flaxseed or soy on estrogen metabolism and biochemical markers of bone metabolism in postmenopausal women. DESIGN: In a parallel design, the diet of postmenopausal women (n = 46) was supplemented with either a placebo, soy (25 g soy flour), or flaxseed (25 g ground flaxseed) muffin for 16 wk. Blood and 24-h urine samples were collected at baseline and at the endpoint. Urine samples were analyzed for phytoestrogens, estrogen metabolites (2-hydroxyestrone, 16alpha-hydroxyestrone), and serum hormones (estradiol, estrone, estrone sulfate). Serum and urine samples were also analyzed for biochemical markers of bone metabolism. RESULTS: Urinary concentrations of 2-hydroxyestrone, but not of 16alpha-hydroxyestrone, increased significantly in the flaxseed group (P = 0.05). In the flaxseed group, the ratio of 2-hydroxyestrone to 16alpha-hydroxyestrone was positively correlated with urinary lignan excretion (r = 0.579, P = 0.02). In the soy and placebo groups, no significant correlation was observed. No significant change in serum hormones or biochemical markers of bone metabolism was observed within or between the treatment groups. CONCLUSIONS: Supplementation with flaxseed modifies urinary estrogen metabolite excretion to a greater extent than does supplementation with an equal amount of soy. This modification by flaxseed is associated with an increase in urinary lignan excretion. Despite the shift in estrogen metabolism to favor the less biologically active estrogens, a negative effect on bone cell metabolism was not observed.

PMID: 14749240 [PubMed – indexed for MEDLINE]

[x] Epidemiology. 2006 Jan;17(1):80-8. Links

Estrogen metabolism and breast cancer.

- ✓ Kabat GC ,
- ✓ O'Leary ES ,
- ✓ Gammon MD ,
- ✓ Sepkovic DW ,
- ✓ Teitelbaum SL ,
- ✓ Britton JA ,
- ✓ Terry MB ,
- ✓ Neugut AI ,
- ✓ Bradlow HL .

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BACKGROUND: Specific pathways involved in estrogen metabolism may play a role in the etiology of breast cancer. We used data from a large population-based case-control study to assess the association of the urinary estrogen metabolites 2-hydroxyestrone (2-OHE1), 16alpha-hydroxyestrone (16-OHE1), and their ratio (2/16) with both invasive and in situ breast cancer. METHODS: Study participants from the Long Island Breast Cancer Study Project provided a spot urine specimen and completed a comprehensive interviewer-administered questionnaire. Women who used exogenous hormones or who took tamoxifen in the 6 months before urine collection were excluded from the analysis, leaving 269 invasive cases, 158 in situ cases, and 326 controls. Unconditional logistic regression was used to obtain adjusted odds ratios (ORs) for invasive and in situ breast cancer, separately, in relation to tertiles of the individual metabolites (standardized for creatinine) and the 2/16 ratio, stratified by menopausal status. RESULTS: The OR for invasive breast cancer was inversely associated with the 2/16 ratio among premenopausal women (OR = 0.50 for extreme tertiles; 95% confidence interval = 0.25-1.01). ORs ranged from 0.32 to 0.60 when women were stratified by whether cases had received chemotherapy within 6 months before urine collection and by estrogen receptor status. In postmenopausal women, there was a slight reduction in the odds ratio for invasive cancer with high levels of the 2/16 ratio (OR = 0.78; 95% confidence interval = 0.46-1.33). Neither the individual metabolites nor the ratio were associated with in situ breast cancer. CONCLUSION: These data provide support for the hypothesis that the 2/16 ratio is associated with reduced breast cancer risk. The most consistent associations were observed with invasive cancer in premenopausal women.

PMID: 16357599 [PubMed – indexed for MEDLINE]

[xi] Eur J Cancer Prev. 2006 Jun;15(3):225-32. Links

Plasma enterolactone and genistein and the risk of premenopausal breast cancer.

- ✓ Piller R ,
- ✓ Chang-Claude J ,
- ✓ Linseisen J .

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BACKGROUND: The scientific debate on the role of dietary phytoestrogens for prevention of breast cancer is still ongoing. We previously reported an inverse association between dietary phytoestrogen intake and premenopausal breast cancer risk and now examine the relationship with plasma phytoestrogen concentrations. METHODS: We measured enterolactone (mammalian lignan) and genistein (isoflavone) concentrations in plasma samples of 220 premenopausal cases and 237 age-matched controls from a population-based case-control study in Germany . RESULTS: Median plasma enterolactone concentrations in cases and controls were 6.3 and 9.7 nmol/l, respectively, and median genistein concentrations were 4.5 and 3.7 nmol/l, respectively. Premenopausal breast cancer risk decreased with increasing plasma enterolactone levels. Adjusted odds ratios (95% confidence intervals) were 0.42 (0.20-0.90) and 0.38 (0.17-0.85) (P for trend 0.007) for women in the third and fourth quartile of plasma enterolactone compared to those in the lowest quartile. There was no significant association between plasma genistein concentration and premenopausal breast cancer risk. CONCLUSION: Using biomarkers of phytoestrogen intake, we confirmed the strong inverse association between enterolactone and premenopausal breast cancer risk as found with dietary intake estimates. This result gives support to the potential role of mammalian lignans for breast cancer prevention among premenopausal women in Western populations.

PMID: 16679865 [PubMed – in process

[xii] Int J Cancer. 2004 Sep 1;111(3):440-3. Links

Dietary lignan intakes and risk of pre- and postmenopausal breast cancer.

- ✓ McCann SE ,
- ✓ Muti P ,
- ✓ Vito D ,
- ✓ Edge SB ,
- ✓ Trevisan M ,
- ✓ Freudenheim JL .

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Lignans are plant compounds metabolized in the mammalian gut to produce the phytoestrogens enterolactone and enterodiol. Because estrogens have been linked to breast cancer etiology, lignans could affect breast cancer risk through modulation of endogenous estrogen metabolism or competitive inhibition with estrogen receptors. We examined breast cancer risk and dietary lignan intake in a population-based case-control study of 1,122 women with primary, incident, histologically confirmed breast cancer and 2,036 controls frequency matched to cases on age and county of residence as part of the Western New York Exposures and Breast Cancer (WEB) Study. Diet was assessed with a self-administered 104-item food frequency questionnaire and other relevant data were collected by detailed in-person interviews. Lignans were expressed as the sum of the dietary precursors secoisolariciresinol and matairesinol. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated by unconditional logistic regression, adjusting for age, total energy and other breast cancer risk factors. Premenopausal women in the highest quartile of dietary lignan intake had reduced breast cancer risk (OR = 0.66; 95% CI = 0.44-0.98). No association was observed between lignan intakes and postmenopausal breast cancer. Our results suggest that dietary lignans may be important in the etiology of breast cancer, particularly among premenopausal women. Copyright 2004 Wiley-Liss, Inc.

PMID: 15221974 [PubMed – indexed for MEDLINE]

[xiii] J Nutr. 2006 Jun;136(6):1596-603. Links

CYP17 genotype modifies the association between lignan supply and premenopausal breast cancer risk in humans.

- ✓ Piller R ,
- ✓ Verla-Tebit E ,
- ✓ Wang-Gohrke S ,
- ✓ Linseisen J ,
- ✓ Chang-Claude J .

Unit of Human Nutrition and Cancer Prevention, Technical University of Munich , Germany .

Cytochrome P450c17alpha (CYP17) has been associated with alterations in steroid hormone levels and premenopausal breast cancer risk and could modify the association between phytoestrogen intake and breast cancer risk. We examined plasma concentrations of enterolactone and genistein, estimated dietary phytoestrogen intake, CYP17 5'-UTR MspA1 genetic polymorphism, and breast cancer risk in 267 premenopausal breast cancer patients and 573 age-matched population controls from Germany. Multivariate logistic regression was used to estimate breast cancer risk associated with quartiles of phytoestrogen intake by genotype and to investigate gene-nutrient interactions. Premenopausal breast cancer risk was not significantly associated with the CYP17 A2 genotype. We observed a significant modifying effect of CYP17 genotype on plasma enterolactone-associated breast cancer risk (P for interaction < 0.01). Plasma enterolactone was significantly inversely related to breast cancer risk only in A2A2 carriers, showing odds ratios and 95% CI of 0.02 (0.00-0.41) and 0.01 (0.00-0.21) for the third and fourth quartiles vs. the lowest quartile, respectively. This inverse association was also found for the calculated enterolignan production as well as matairesinol intake. Compared with A1A1 carriers with the lowest enterolactone supply, the risk reduction associated with a high enterolactone supply resulted in a comparably decreased breast cancer risk for all genotypes. For genistein, no clear indication for a differential effect by CYP17 genotype was obtained. Our results suggest that CYP17 genotype modifies the protective effect of lignans on premenopausal breast cancer risk. Women homozygous for A2 allele benefit most from high plasma enterolactone concentrations and a high consumption of dietary precursors.

PMID: 16702327 [PubMed – indexed for MEDLINE

[xiv] J Nutr. 2002 Oct;132(10):3036-41. Links

The risk of breast cancer associated with dietary lignans differs by CYP17 genotype in women.

- ✓ McCann SE ,
- ✓ Moysich KB ,
- ✓ Freudenheim JL ,
- ✓ Ambrosone CB ,
- ✓ Shields PG .

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Lignans are plant compounds metabolized in the gut to produce the phytoestrogens enterolactone and enterodiol. Reduced breast cancer risks associated with higher urinary lignan excretion may be related to competitive inhibition of endogenous estrogens. Evidence exists that associations with reproductive risk factors for breast cancer differ according to cytochrome P450c17alpha (CYP17) genotype. Genetic variability in estrogen metabolism could alter lignan metabolism thereby modifying risk associations. We examined breast cancer risk, dietary lignans and CYP17 genotype among 207 women with primary, incident, histologically confirmed breast cancer and 188 controls frequency matched to cases by age and county of residence. Self-reported frequency of intake of 170 foods and beverages during the 2 y before the interview and other relevant data were collected by detailed in-person interviews. Dietary lignan intake was expressed as the sum of enterolactone and enterodiol production from foods. Odds ratios (OR) and 95% confidence intervals (CI) were estimated by unconditional logistic regression, adjusting for age, education and other breast cancer risk factors. Women in the highest tertile of dietary lignans tended to have reduced breast cancer risk (OR 0.45, 95% CI 0.20-1.01 and OR 0.59, 95% CI 0.28-1.27, pre- and postmenopausal women, respectively). Substantially reduced risks in the highest tertile of lignans were observed for premenopausal women with at least one A2 allele (OR 0.12, 95% CI 0.03-0.50). Our results suggest that CYP17 genotype may be important in modifying the effect on breast cancer risk of exogenous estrogens, particularly for premenopausal women.

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Flax seeds, especially flax seeds ground into meal, are useful for preventing breast cancer and also useful in treating existing cancer. Yet twice in the last week, I have answered emails from patients with breast cancer inquiring if flax seeds were still ok to eat. Lately there is this, to use the new word, buzz about flax seeds. An idea is going around that flax seeds are no longer ok. Supposedly, "experts" are recommending women with breast cancer stop eating flax seeds. To quote my esteemed colleague, Dr. Michael Uzick,

"This recommendation is based solely on a notion, rather than scientific evidence. The logic behind this notion is that the weak phytoestrogens contained in flax seeds could potentially stimulate hormone dependent cancers in postmenopausal women with a history of breast cancer. However, this "logic" is specious since all the evidence from scientific research show the complete opposite to be true."

The buzz no doubt stems from a study published in the November 15, International Journal of Cancer. Researchers fed pregnant rats diets high in either wheat, oats, or defatted flax seeds. When the offspring of these rats were about 7 weeks old, they were dosed with DMBA, a cancer causing drug, and watched to see how many developed breast cancer. The baby rats whose mothers had eaten whole wheat had a lower than average risk of getting cancer, the descendents of the flax meal fed rats had a slightly higher incidence. The study's conclusion that, "… maternal dietary exposure to whole wheat during pregnancy may reduce offspring's breast cancer risk by improving DNA damage repair mechanisms." doesn't focus on increased risk from flax seed consumption at all but rather the protection from whole wheat .

[i] This study is about rats, and actually offspring of rats. It is difficult to extrapolate rat dietary data to humans, especially human women with breast cancer. At best, we might garner that women shouldn't eat excessive amounts of flax seed while pregnant. The clearer message is that whole-wheat flour should be encouraged during pregnancy.

The question of what flax seed does for a woman with breast cancer or at high risk of breast cancer is not addressed in this study. On the other hand, there are significant studies that do provide useful answers.

Flax seed muffins:

One and half cups whole wheat flour
One and a half cups ground flax meal
1 TB baking powder
one half tsp nutmeg
one half tsp ginger
two tsp cinnamon

one and a half cups milk
one half cup honey
2 eggs beaten

one half or so cups raisins
1 cup or so grated carrots

Whisk dry ingredients together, beat wet ingredients together, mix both together the dry and wet ingredients, then fold in the remaining items.

Bake at 350 degrees in muffin tins lined with paper, about 25 minutes

http://www.denvernaturopathic.com/news/flaxseeds.html

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